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HEPATITIS C VIRUS GENOTYPES IN PATIENTS AND BLOOD DONORS — QUEBEC

Hepatitis C is currently and will continue to be an important public health problem worldwide. Seroprevalence rates in blood donors range from 0.05% to 2.5%[1,2]. An exceptionally high rate (13% to 20%) is encountered in Egyptian donors and the reason for this remains unknown[3]. In North America, the seroprevalence rate among volunteer blood donors varies from 0.05% to 0.7%[4]. In the general population the rate is believed to be higher than that found in blood donors since the latter are initially screened for risk factors and hepatitis C seroposivity[4]. In the United States, 150,000 cases of hepatitis C virus (HCV) infections are estimated to have occurred annually over the past 10 years[5]. HCV infection is characterized by its high rate of chronicity; 60% to 80% of infected individuals develop chronic liver disease of varying degrees of severity, including cirrhosis in 20% of cases and, more rarely, hepatocellular carcinoma.

Distinct genomic variants of HCV have been identified with different geographic distributions[6]. Phylogenetic analysis of nucleotide sequences from isolates worldwide show that they cluster into major groups. Isolates within major groups may in turn cluster into additional groups (subgroups). A system of nomenclature designating major groups as types and subgroups as subtypes has been proposed[7]. The genotypes referred to in this report correspond to those assigned by this classification scheme. Infection with different HCV genotypes may have clinical significance. For instance, there is increasing evidence suggesting that the response to interferon therapy differs among some of the genotypes. In addition, genotypes may influence the clinical course of infection[8].

In Canada, the existence of various HCV genotypes has been recently documented[9-12] and two studies report prevalence rates[10,11]. The first documents the presence of six major HCV types in a limited number (n = 46) of blood donors[10]. The second reports data for only two of the major types (1 and 2) and their subtypes in various risk groups and blood donors[11]. These studies show that type 1 accounts for more than 50% of HCV infections.

In this study, we have analyzed the distribution of the major HCV types among 132 viremic patients followed at the hepatology unit of Hôpital Saint-Luc in Montreal between 1991 and 1994 and 132 viremic voluntary blood donors from the Montreal area found anti-HCV positive by RIBA 2.0 (Chiron Corporation, Emeryville, CA) between 1992 and 1994. HCV RNA was detected in serum of patients and donors by reverse-transcription polymerase chain reaction[9]. Genomes were typed by restriction fragment length polymorphism analysis of amplified 5' noncoding region (NCR) sequences according to an updated version of our previously described procedure[10]. In addition, nucleotide sequence analysis of amplified 5' NCR sequences was performed as confirmatory assay for one unclassifiable type (putative new type). Typing results are shown in Table 1.

The distribution of genotypes between patients and blood donors was not significantly different ($p > 0.05$). In both groups, type 1 was predominant followed by type 2 and type 3, respectively; these three types together accounted for 88% of the isolates in patients and 92% of the isolates in donors. Types 4 and 5 were also found in both groups. A single type 6 was found in a blood donor and a putative new type was found among one of the patients. Most of the persons infected with types 1, 2, and 3 were of Canadian origin. Eleven of the 12 persons infected with type 4 were immigrants from Africa or the Middle East. This is not surprising since type 4 is found mainly in Egypt, the Middle East and Central Africa[6]. The other patient infected with type 4 is of Canadian origin. This patient reported intravenous (IV) drug use as risk factor and no travel history to Africa or the Middle East. Surprisingly, we found 12 persons of Canadian and one of European origin to be infected with type 5. Type 5 isolates have been previously encountered in patients and donors from South Africa and rarely elsewhere. A travel history to South Africa was not reported by these individuals. Six reported receiving blood products as risk factor. Sexual/household contact, IV drug use, acupuncture and tattooing were each reported once, while in three the mode of transmission remained unknown. The person with sexual/household contact as risk factor is the spouse of one of the

six who reported receiving blood products. The donor infected with a type 6 isolate is an immigrant from Vietnam, an area where additional type 6 isolates have been found[13]. The patient infected with a putative new type immigrated to Canada from Somalia (East Africa). Thus, 1, 2, 3, and 5 are the principal types transmitted in Canada while other types are mostly encountered in persons who acquired the infection outside of Canada.

Type 2 is the second predominant genotype in the Montreal area with a prevalence of 15%. This is noteworthy since patients infected with type 2 appear to respond better to interferon therapy and to have lower serum HCV RNA levels than their type 1 infected counterparts. Since the distribution of HCV types between patients and asymptomatic blood donors is similar, it may be tempting to hypothesize that the types do not associate with different disease severities. However, patients followed also include asymptomatic individuals referred solely on the basis of elevated serum aminotransferases or a positive serology. Histologic examination of blood donors is underway to assess the relationship between genotypes and disease severity. Two recent studies in American patients report rates of 75% to 80%, 15%, and 5% to 6% for types 1, 2, and 3, respectively[14,15]. This distribution is different from that observed among our patients ($p < 0.05$) and may be explained by the higher frequency of types other than 1, 2, and 3 and by a lower frequency of type 1 in the Montreal area. Note that only one of the two studies in American patients would have been able to identify type 5 genomes, if present, and none were reported[15]. Identification of HCV genotypes will allow the correlation with clinical courses and may be helpful for studying epidemiologic outbreaks of HCV and in identifying sources of transmission.

Recent data from Vietnam indicate the existence of three new types (7, 8, and 9) contributing to 20% of types found in that country[13]. These new types have 5' NCR sequences indistinguishable from that of type 1 isolates. Sequence analysis of the coding regions of numerous isolates worldwide, including a substantial number from the United States[15], would indicate that these isolates are seldom found outside of Vietnam. Therefore, types 7, 8, and 9 are expected to be rare in Quebec.

Knowledge of the distribution of HCV genotypes is of importance considering that efforts are being made towards the development of a vaccine[16]. The occurrence of different genotypes could represent a problem since an immune response towards one genotype may not protect against infection with a different genotype. Unfortunately, the existence of HCV variants is not the only concern in the development of a vaccine. Of great worry is the observation that infection may not protect from reinfection with a homologous genotype[17]. The high level of chronicity observed indicates that in most persons a protective immunity does not develop. An understanding of the factors involved in the establishment of immunity will be important for devising an effective vaccine. Public awareness of the consequences of acquiring HCV infection and of the risk factors for transmission will continue to play an important role in the fight against hepatitis C.

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Table 1
Distribution of the major HCV types in patients and blood donors, Hepatology Unit, Hôpital Saint-Luc, Montreal 1991 to 1994

Group	Sample size	HCV types (%)													
		1		2		3		4		5		6		Other	
Patients	132	87	(65.9)	16	(12.1)	13	(9.8)	9	(6.8)	6	(4.5)	0		1	(0.8)
Blood donors	132	77	(58.3)	25	(18.9)	19	(14.4)	3	(2.3)	7	(5.3)	1	(0.8)	0	
Total	264	**164**	**(62.1)**	**41**	**(15.5)**	**32**	**(12.1)**	**12**	**(4.5)**	**13**	**(4.9)**	**1**	**(0.4)**	**1**	**(0.4)**

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Source: *DG Murphy, PhD, B Willems, MD, G Delage, MD, MSc, D Fenyves, MD, PM Huet, MD, PhD, D Marleau, MD, MSc, G Pomier-Lavrargues, MD, J-P Villeneuve, MD, MSc, and J Vincelette, MD, MSc. Laboratoire de santé publique du Québec, Sainte-Anne-de-Bellevue, Quebec; Hepatology Unit and Microbiology and Infectious Disease Unit, Hôpital Saint-Luc, Montreal, Quebec.*

SEROPREVALENCE OF HEPATITIS C IN A CANADIAN FEDERAL PENITENTIARY FOR WOMEN

Introduction

A recent study of hepatitis C seroprevalence among volunteers in a male federal penitentiary in Western Canada showed a seropositivity rate of 25% among the 23% of prisoners who volunteered to be tested[1]. The main mode of transmission of hepatitis C is either blood transfusion or intravenous (IV) drug use with sexual transmission a less likely possibility[1,2]. Apart from the above study there is currently no published information concerning the seroprevalence rate for hepatitis C in North American prisons.

We report a voluntary linked, anonymous cross-sectional study of hepatitis C carried out in the Federal Prison for Women at Kingston, Ontario, in conjunction with a study of HIV seroprevalence in the same population.

Methods

The study protocol was similar to that used for the HIV-1 seroprevalence study carried out in Joyceville Penitentiary in April of 1993[3]. The original intent was to test solely for HIV serology, but during the pretesting educational sessions the prisoners asked that we also test for hepatitis C and the protocol and pretest educational sessions were changed accordingly.

Pretest education sessions included viewing a video of the Joyceville study and group meetings with one of the study physicians, an AIDS project worker and a social worker to talk about both HIV and hepatitis C. Educational material on HIV and hepatitis C prepared for the study was also distributed to all prisoners.

In May 1994 the prison was shut down for the day while blood samples were taken. The phlebotomy team consisted of a physician, two nurses, a social worker and two workers from the AIDS projects. Individual pretest counselling was available for each volunteer. A perforated label with an identical number on each half was used. One half was attached to the tube of blood and the other half given to the donor. The individual result was placed in a sealed envelope and the number put on the outside. An individual could obtain her result on presentation of the appropriately numbered label.

No attempt was made to evaluate risk behaviour as it was made clear by inmate representatives that this would jeopardize the participation rate.

Blood samples were sent to the Kingston Public Health Laboratory, Ontario Ministry of Health, for testing. Samples tested for hepatitis C were screened by Ortho 3.0 ELISA, and positives and "grey zone" specimens were further tested using the third generation Organon Technika UBV HCV EIA and/or the Chiron RIBA HCV 3.0 assay. Hepatitis C testing was performed at the Central Public Health Laboratory, Ontario Ministry of Health, Toronto.

A social worker or AIDS project worker was available for counselling when results were handed out and for 2 weeks after.

Results

The Prison for Women at Kingston houses both medium and maximum security prisoners. Length of sentence ranges from 2 to 20 years with the majority serving less than 5 years. Ages range from 18 to over 50 with the majority falling between 25 and 40. On the day of the study the prison population was 130 and 113 volunteered for testing (86.9%). Forty-five women tested positive for hepatitis C (39.8%). One individual was positive for hepatitis B surface antigen.

Hepatitis B antibody testing is not reported because a hepatitis B immunization program was in progress and the results of antibody testing were not interpretable.

All volunteers collected a label and all but eight collected their results.

Comment

The response rate was excellent at 86.9% and we feel that at this rate there is only a small risk of results being seriously biased due to high-risk individuals avoiding being tested.

The figure of 39.8% for hepatitis C seroprevalence is disturbingly high. Hepatitis C is generally spread by either blood transfusion or by the use of contaminated injection equipment with sexual transmission being a more remote possibility. Seropositivity for hepatitis C in this population likely represents a marker for IV drug use at some time in the majority of those testing positive and suggests an alarming potential for the rise of HIV in the future should the prevalence of HIV increase in the incoming population. Urgent measures are needed to address the problem of IV drug use in prison populations.

All the prisoners were told that, following the study, further investigation and, if appropriate, treatment would be available to

those who appeared to have active disease as a consequence of hepatitis C infection. This would involve all those who knew they were positive on study results and any others wishing to be tested coming forward for non-anonymous (nominal) testing. This follow-up is currently being carried out and, as of this time, around 90% of the population has presented for nominal testing.

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Source: *PM Ford, MB, FRCP, Department of Medicine, Queen's University; C White, BA, MA, Prison Outreach Worker, Kingston AIDS Project; H Kaufmann, BA, MSc, Social Worker, AIDS Clinic, Kingston General Hospital; J MacTavish, Support Services Coordinator, Kingston AIDS Project; M Pearson, MD, CCFP, Prison Physician and Lecturer, Department of Family Medicine, Queen's University; S Ford, MB, FRCP, Departments of Medicine and Pathology, Queen's University; PS Mistry, DSc, Director, Kingston Public Health Laboratory, Ontario Ministry of Health; P Connop, MB, FRCP, Prison Physician and Associate Professor, Departments of Community Health and Epidemiology, Queen's University, Kingston, Ontario.*

VOLUNTARY SCREENING FOR HEPATITIS C IN A CANADIAN FEDERAL PENITENTIARY FOR MEN

We recently carried out a voluntary linked, anonymous study of hepatitis C seroprevalence in the Federal Prison for Women at Kingston, Ontario (see second article in this issue). One hundred and thirteen inmates (86.9%) of the prison population volunteered to be tested and 39.8% were found positive for antibodies to hepatitis C.

An increasing awareness of hepatitis C among inmates of other penitentiaries in the area led to a rise in the number of prisoners requesting testing. It was therefore decided to offer hepatitis C testing on a voluntary nominal basis to the entire population of a male penitentiary. The penitentiary selected was Joyceville, a medium security federal penitentiary at Kingston. This penitentiary had been the site of a linked anonymous study of the seroprevalence of HIV[1] carried out in 1993. On this occasion, because of the concern that prisoners had who had heard of the results of the study at the women's prison, and to avoid having to repeat the testing, inmates were tested on a nominal basis.

Methods

Prisoners were informed about the availability of testing at educational sessions where a physician addressed the prison population in groups, distributed educational materials and answered questions. In addition, an informational video program, made with the same physician by the inmate film unit, was shown on the prison television system. It was made clear that all prisoners who tested positive for hepatitis C would be further investigated, if they wished, and assessed as to their suitability for treatment. It was emphasized that the testing was voluntary.

For 2 days the prison was shut down and two teams, each comprised of a physician and two nurses, collected blood samples from volunteers. Each tube was labelled with the name and number of the volunteer.

Screening for hepatitis C antibodies was carried out by the Public Health Laboratory in Ottawa, and confirmatory testing was performed by the Central Public Health Laboratory, Ontario Ministry of Health in Toronto, as described in the second article.

As soon as they were available, the results were sent to the appropriate donors in sealed envelopes and all those who tested positive were invited to go to the prison health care facility for further testing, if they wished.

Results

The prison population on the day of testing was 592; blood samples were obtained from 408 prisoners for a response rate of 68.9%. On these 408 individuals, 114 (27.9%) were positive for hepatitis C antibodies.

Comment

The response rate of 68.9% was good. We feel that volunteer bias was, if anything, slanted towards high-risk individuals because a number of prisoners informed us that they were not going to give a blood sample because they had not been involved in any risk behaviour.

The seropositivity rate of 27.9% is somewhat lower than that found in the women's prison. This may reflect a different exposure to risk prior to incarceration in female compared to male prisoners. Hepatitis C seropositivity in this population likely represents a marker for intravenous drug use. Infection may well have occurred prior to incarceration, but this finding does indicate a significant population with a propensity to high-risk behaviour. It also indicates a considerable burden of ill health which will fall, initially, on the prison medical services but, ultimately, on provincial health care systems.

These results would emphasize, yet again, the need to implement the harm-reduction strategies outlined in the report of the Expert Committee on AIDS and Prisons[2].

Follow-up of seropositives is currently being carried out.

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Source: *M Pearson, MD, CCFP, Prison Physician and Lecturer in the Department of Family Medicine, Queen's University; PS Mistry, DSc, Director, Kingston Public Health Laboratory, Ontario Ministry of Health; PM Ford, MB, FRCP, Department of Medicine, Queen's University, Kingston, Ontario.*

Editorial Comment: These three articles add to the paucity of epidemiologic information available on hepatitis C in Canada. The major mode of transmission at present is injection drug use (IDU). The magnitude of the prevalence of hepatitis C in a high-risk population is confirmed by the studies carried out in Kingston. The previous study of male inmates carried out in British Columbia showed a prevalence of 28% with a relative risk of 3.4 for IDU[1]. The male inmates in Kingston show an identical rate. The high prevalence in women (39.8%) is probably indicative of the risk profile of the female inmate population. It will be necessary to explore further both the specific circumstances of infection, primarily related to drug use and perhaps sexual activity, and the independent risk of tattooing and other skin piercing activities. The incidence of infection among inmates while in prison will also have to be examined. Those concerned about the issue of prisoners' health should refer to the report on HIV/AIDS in prisons, as noted by the authors. Hepatitis C in high-risk populations will be a good indicator of the possibility of HIV transmission.

The burden of illness in Canada has yet to be clearly defined. An important unanswered question relates to the natural history of the disease, especially in those acquiring the infection as young adults through IDU. The severity of disease may depend on genotype and/or the virus load. The Montreal study adds to the evidence that the predominant genotype acquired in Canada is type 1. The significance of this with regard to the likely success of treatment and severity of disease in this country is not yet clear. However, it is interesting to note that the prevalence of type 1 in healthy blood donors is no different from that found in hepatology unit patients.

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